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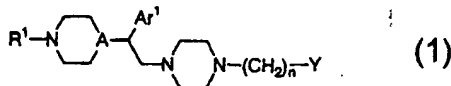
(10) 国際公開番号
WO 03/053927 A1

- (51) 国際特許分類: C07D 209/48, 211/26, 231/12, 233/70, 233/84, 239/26, 239/42, 261/08, 263/32, 277/40, 277/56, 295/12, 295/14, 307/91, 313/18, A61K 31/496, 31/517, A61P 3/04, 25/22, 25/24, 43/00
- (71) 出願人 (米国を除く全ての指定国について): 大正製薬株式会社 (TAISHO PHARMACEUTICAL CO.,LTD.) [JP/JP]; 〒170-8633 東京都豊島区高田3丁目2番1号 Tokyo (JP).
- (21) 国際出願番号: PCT/JP02/13317
- (72) 発明者; および
- (22) 国際出願日: 2002年12月19日 (19.12.2002)
- (73) 発明者/出願人 (米国についてのみ): 中里 篤郎 (NAKAZATO, Atsuro) [JP/JP]; 〒170-8633 東京都豊島区高田3丁目2番1号 大正製薬株式会社内 Tokyo (JP). 石井 孝明 (ISHII, Takaaki) [JP/JP]; 〒170-8633 東京都豊島区高田3丁目2番1号 大正製薬株式会社内 Tokyo (JP). 野沢 大 (NOZAWA, Dai) [JP/JP]; 〒170-8633 東京都豊島区高田3丁目2番1号 大正製薬株式会社内 Tokyo (JP).
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特願 2001-389419
2001年12月21日 (21.12.2001) JP

[続葉有]

(54) Title: PIPERAZINE DERIVATIVE

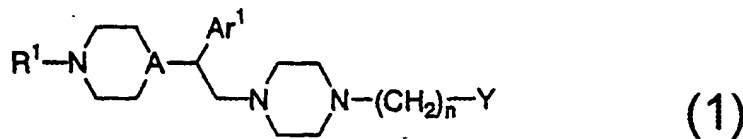
(54) 発明の名称: ピペラジン誘導体



(57) Abstract: A piperazine derivative represented by the formula (1) [wherein n is an integer of 1 to 8; R¹ represents hydrogen or C₁₋₁₀ alkyl; A represents CH or nitrogen; Ar¹ represents phenyl or substituted phenyl; and Y represents a group represented by the formula Y¹-Y²-Ar² or Y³-Y⁴(Ar⁵)-Ar⁶ or a pharmaceutically acceptable salt of the derivative. The novel piperazine derivative has MC₄ receptor antagonistic activity.

(57) 要約:

式



(式中、nは1～8の整数を示し、R¹は水素原子又はC₁₋₁₀アルキル基を示し、AはCH又は窒素原子を示し、Ar¹はフェニル基又は置換フェニル基を示し、Yは式Y¹-Y²-Ar²又は式Y³-Y⁴(Ar⁵)-Ar⁶で表される基である。)で表されるピペラジン誘導体又はその医薬上許容される塩。

MC₄受容体アンタゴニスト作用を有する新規ピペラジン誘導体を提供する。

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- (81) 指定国 (国内): AE, AG, AI, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) 指定国 (広域): ARIPO 特許 (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), ユーラシア特許 (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), ヨーロッパ特許 (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI 特許 (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

添付公開書類:

— 国際調査報告書

2文字コード及び他の略語については、定期発行される各PCTガゼットの巻頭に掲載されている「コードと略語のガイダンスノート」を参照。

明 細 書

ピペラジン誘導体

技術分野

本発明は、MC 4 受容体アンタゴニストを有効成分とする不安神経症又はうつ症治療薬、及びMC 4 受容体アンタゴニスト作用を有する新規ピペラジン誘導体に関する。

背景技術

最近の病態生理学の進歩により、不安神経症及びうつ病の発症機序としてストレスが深く関与していることが示唆されている。ストレスにより引き起こされる脳内反応としては、視床下部一下垂体-副腎系の機能異常を代表とする神経内分泌系の機能異常が知られている。このような背景から、最近、視床下部に存在し、神経内分泌系に影響を与える神経ペプチドがうつ・不安の発症原因として注目されている。

このような神経ペプチドとして、コルチコトロピン・リリーシング・ファクター (CRF)、プロオピオメラノコルチン (POMC) 等が挙げられる。POMC から生成されるメラノコルチン類 [副腎皮質刺激ホルモン (ACTH)、メラニン細胞刺激ホルモン (MSH)] は視床下部における主要な神経ペプチドであるが、メラノコルチン受容体に作用する物質についてのストレス反応及びうつ・不安症への関与は報告されていない。

メラノコルチン受容体はMC 1~MC 5まで5つのサブタイプに分類される。これらのサブタイプの中でメラノコルチン受容体サブタイプMC 4に関して、ペプチド性の選択的アゴニスト及びアンタゴニストが報告されているものの、非ペプチド性のアゴニスト及びアンタゴニストに関しては全く報告されていない。

本発明の目的は、メラノコルチン受容体のサブタイプMC 4に対しアンタゴニスト作用を有する新規な化合物を提供することにある。

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP02/13317

<p>A. CLASSIFICATION OF SUBJECT MATTER Int.Cl⁷ C07D209/48, 211/26, 231/12, 233/70, 233/84, 239/26, 239/42, 261/08, 263/32, 277/40, 277/56, 295/12, 295/14, C07D307/91, 313/18, A61K31/496, 31/517, A61P3/04, 25/22, 25/24, 43/00 According to International Patent Classification (IPC) or to both national classification and IPC</p>													
<p>B. FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) Int.Cl⁷ C07D209/48, 211/26, 231/12, 233/70, 233/84, 239/26, 239/42, 261/08, 263/32, 277/40, 277/56, 295/12, 295/14, C07D307/91, 313/18, A61K31/496, 31/517, A61P3/04, 25/22, 25/24, 43/00 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) CAPLUS, REGISTRY (STN)</p>													
<p>C. DOCUMENTS CONSIDERED TO BE RELEVANT</p> <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>P, X</td> <td>WO 02/00259 A1 (TAISHO PHARM. CO., LTD.), 03 January, 2002 (03.01.02), & AU 2001066342 A</td> <td>1-12, 14</td> </tr> <tr> <td>A</td> <td>WO 96/05185 A1 (MITSUBISHI CHEM. CORP.), 22 February, 1996 (22.02.96), & CA 2197172 A & EP 777660 A1 & CN 1164856 A & JP 10-508826 A</td> <td>1-12, 14</td> </tr> <tr> <td>A</td> <td>EP 310268 A2 (AMERICAN HOME PRODUCTS CORP.), 05 April, 1989 (05.04.89), & US 4826844 A & ZA 8806798 A & AU 8822155 A & GB 2210366 A & CA 1301757 A & JP 1-121281 A</td> <td>1-12, 14</td> </tr> </tbody> </table>		Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	P, X	WO 02/00259 A1 (TAISHO PHARM. CO., LTD.), 03 January, 2002 (03.01.02), & AU 2001066342 A	1-12, 14	A	WO 96/05185 A1 (MITSUBISHI CHEM. CORP.), 22 February, 1996 (22.02.96), & CA 2197172 A & EP 777660 A1 & CN 1164856 A & JP 10-508826 A	1-12, 14	A	EP 310268 A2 (AMERICAN HOME PRODUCTS CORP.), 05 April, 1989 (05.04.89), & US 4826844 A & ZA 8806798 A & AU 8822155 A & GB 2210366 A & CA 1301757 A & JP 1-121281 A	1-12, 14
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<p><input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.</p>													
<p>* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family</p>													
<p>Date of the actual completion of the international search 04 March, 2003 (04.03.03)</p>	<p>Date of mailing of the international search report 18 March, 2003 (18.03.03)</p>												
<p>Name and mailing address of the ISA/ Japanese Patent Office</p>	<p>Authorized officer</p>												
<p>Facsimile No.</p>	<p>Telephone No.</p>												

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP02/13317

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/35878 A1 (AMERICAN HOME PRODUCTS CORP.), 22 June, 2000 (22.06.00), & AU 200031231 A & BR 9916185 A & EP 1140838 A1 & JP 2002-532473 A	1-12, 14
A	WO 99/55695 A1 (AMERICAN HOME PRODUCTS CORP.), 04 November, 1999 (04.11.99), & AU 9939670 A & US 6066637 A & EP 1073651 A1 & CN 1307573 A & JP 2002-513016 A	1-12, 14
A	WO 97/28140 A1 (FABRE MEDICAMENT SA PIERRE), 07 August, 1997 (07.08.97), & FR 2744448 A & AU 9716070 A & EP 886636 A1 & BR 9707261 A & CN 1212690 A & NZ 331221 A & JP 2000-504004 A	1-12, 14
A	EP 479546 A2 (JOHN WYETH & BROTHER LTD.), 08 April, 1992 (08.04.92), & GB 2248616 A & AU 9184883 A & CA 2052619 A & PT 99134 A & US 5177078 A & NZ 240049 A	1-12, 14

INTERNATIONAL SEARCH REPORT

International application No.

PCT/JP02/13317

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 13
because they relate to subject matter not required to be searched by this Authority, namely:
The invention as set forth in claim 13 is relevant to method for treatment of the human body by therapy.

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

- Remark on Protest The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.